A systematic review and meta-analysis of randomized controlled trials exploring the role of inter-individual variability on the effect of flavanols on insulin and HOMA-IR

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Introduction

Meta-analyses of randomised controlled trials (RCTs) report that polyphenol-rich diets can modulate a range of cardiometabolic biomarkers (1, 2). specifically – flavonol, flavanol, anthocyanin and ellagitannins (3).

Inter-individual factors (e.g. age, BMI, ethnicity) may contribute toward the variability in the response to the bioactive.

Scope of the Review

1. To assess the effect of flavanols from cocoa, apple and tea on fasting insulin and HOMA-IR
2. To explore the role of inter-individual variability

Methods

- PubMed & Web of Science were searched from inception to October 2017 (PROSPERO reg. CRD42016033878).
- Estimation of effect of flavanols supplementation on insulin and HOMA-IR using a random effects meta-analysis model
- reported as standardised difference in mean (SDM) and 95%CI.
- Multivariate meta-regression: impact of baseline BMI, gender, age, & study location - the standardised coefficient β was reported, alongside 95% CI
- Evaluation of risk of bias with the Cochrane Collaboration tool modified to include source of funding, baseline comparability.

Results

- 1409 studies screened → 31 RCTs were included reporting on insulin (n=1792); 21 RCTs reporting on HOMA-IR (n=1152).
- Study duration ranged from 2 to 26 weeks and flavanols' doses ranged from 88 to 1344 mg/day.
- Studies followed most often a parallel design; insulin (n=21), HOMA-IR (n=14), with some cross-over studies; insulin (n=10), HOMA-IR (n=7)
- Sample size varied from 23 to 104 for parallel design studies, and 12 to 69 for cross-over design studies.
- 37 RCTs were of moderate risk of bias while 15 were of high risk
- Low heterogeneity between studies (insulin I^2=0%, p=0.98, HOMA-IR I^2=5.9%, p=0.38) but evidence of potential publication bias (HOMA-IR p=0.000, insulin p=0.005).
- **Flavanol-rich interventions decreased both insulin (SDM -0.25, 95%CI -0.33; -0.16, Fig1A) and HOMA-IR (SDM -0.26; 95%CI -0.36, -0.16, Fig1B).**

Multivariate meta-regression:

1. No discernible effect of age, gender, baseline BMI, study location on the insulin response to flavanols.
2. Baseline BMI (overweight but not obese vs lean, β -1.07; 95%CI: -2.03, -0.08; p=0.03) and study location (Asia versus other sites β 0.94; 95%CI: 0.03,1.84; p=0.04) influenced HOMA-IR response to flavanols.

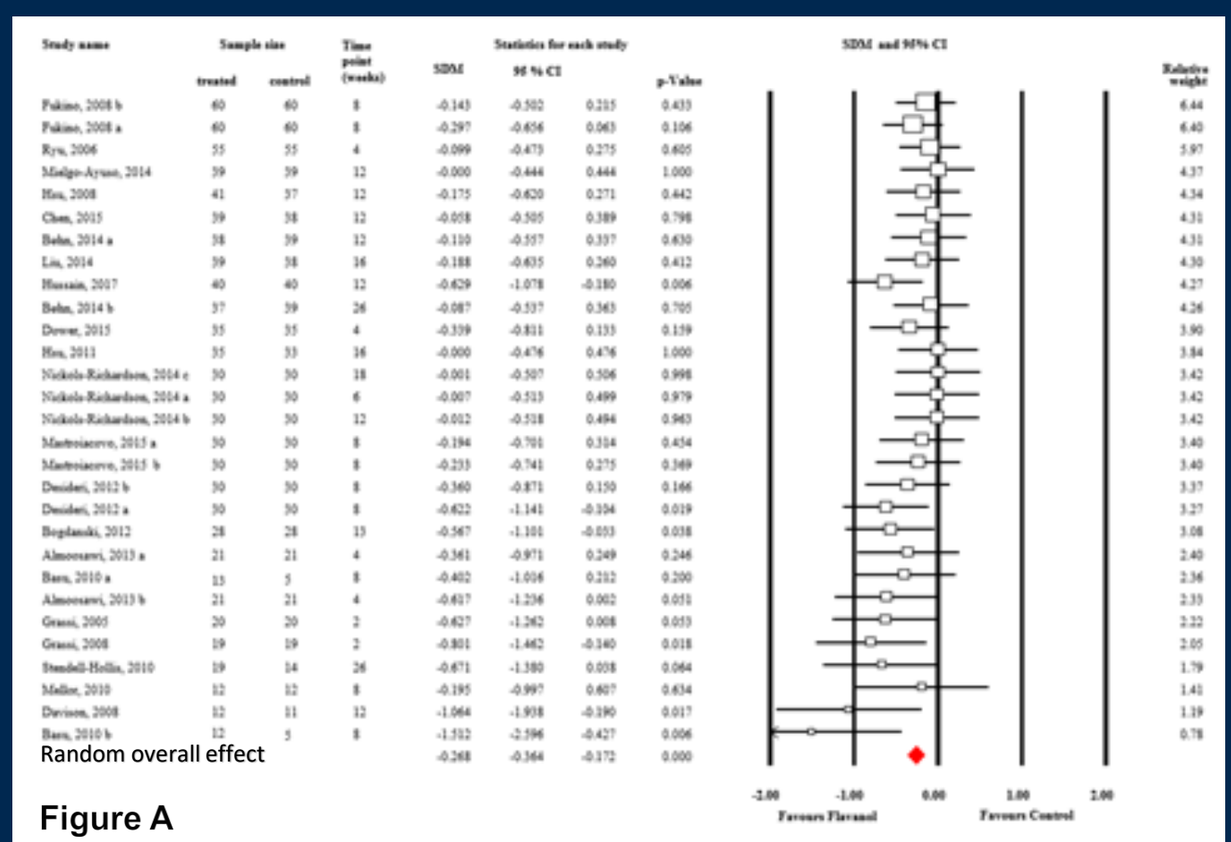

Figure A

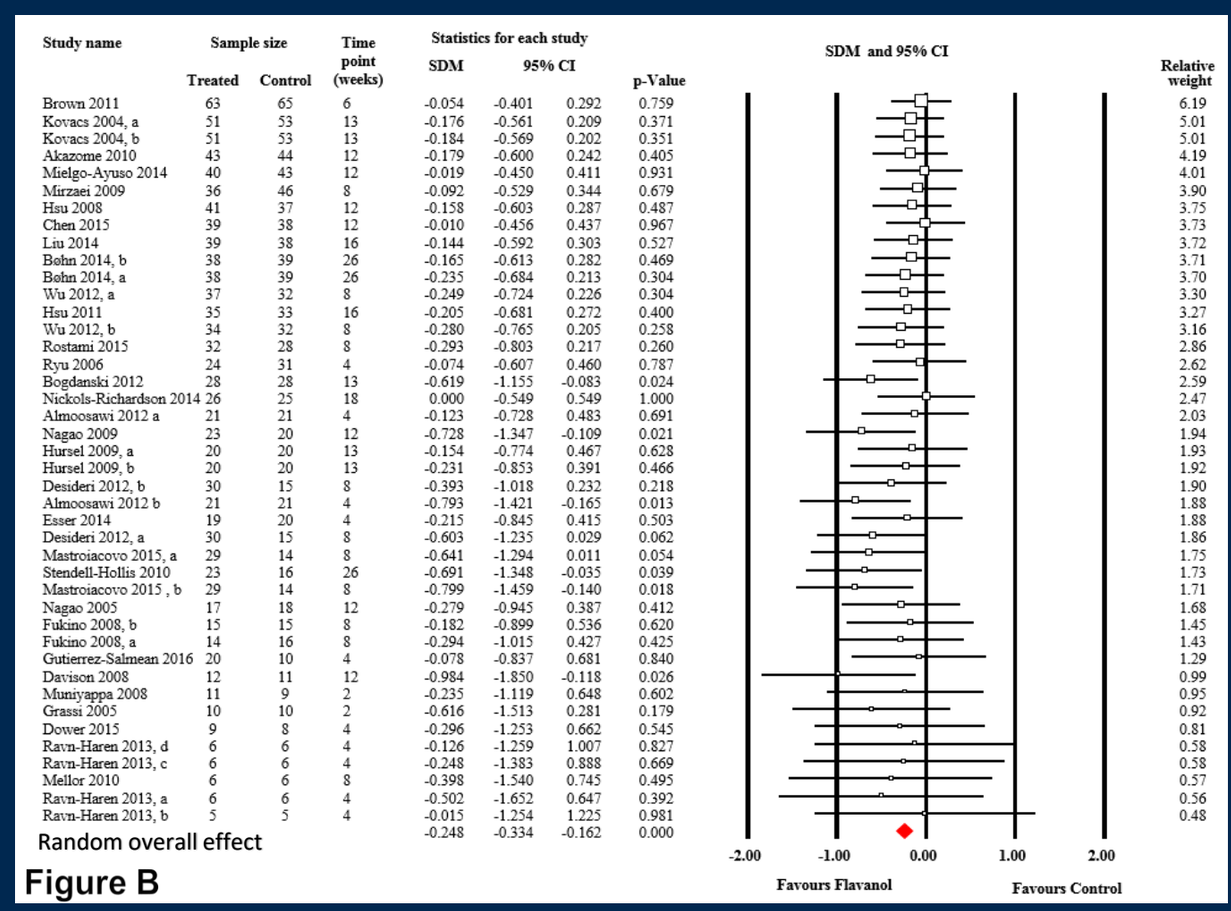

Figure B

Figure 1A & B: Forest plot of the effect of flavanol-containing products on HOMA_IR (A) and insulin (B)

SDM: standardised mean difference, CI: confidence interval

Conclusions

- Flavanols from tea, apple and cocoa promote small but beneficial changes on insulin and HOMA-IR and may contribute to prevent cardiometabolic diseases risk factors.
- Inter-individual variability of insulin in the response to flavanols was limited for insulin compared to other cardiometabolic biomarkers (1,2)
- This could be partly explained by 1) small number of trials reporting data for specific subgroups(e.g gender, medication use) 2) broad range of doses and duration tested among the studies.

Reference

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3. García-Conesa M, Chambers K, Combet E, et al. Int J Mol Sci. 2018;19(3):694.

Acknowledgement

This poster is based upon work from COST Action FA1403-POSITIVe, supported by COST (European Cooperation in Science and Technology) "COST is supported by the EU Framework Programme Horizon 2020"